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2019 American Heart Association Focused Update

- Neonatal Resuscitation
- Pediatric Basic Life Support
- Pediatric Advanced Life Support

An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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2019 American Heart Association Focused Update on Neonatal Resuscitation: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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abstract

This 2019 focused update to the American Heart Association neonatal resuscitation guidelines is based on 2 evidence reviews recently completed under the direction of the International Liaison Committee on Resuscitation Neonatal Life Support Task Force. The International Liaison Committee on Resuscitation Expert Systematic Reviewer and content experts performed comprehensive reviews of the scientific literature on the appropriate initial oxygen concentration for use during neonatal resuscitation in 2 groups: term and late-preterm newborns (≥35 weeks of gestation) and preterm newborns (<35 weeks of gestation). This article summarizes those evidence reviews and presents recommendations. The recommendations for neonatal resuscitation are as follows: In term and late-preterm newborns (≥35 weeks of gestation) receiving respiratory support at birth, the initial use of 21% oxygen is reasonable. One hundred percent oxygen should not be used to initiate resuscitation because it is associated with excess mortality. In preterm newborns (<35 weeks of gestation) receiving respiratory support at birth, it may be reasonable to begin with 21% to 30% oxygen and to base subsequent oxygen titration on oxygen saturation targets. These guidelines require no change in the Neonatal Resuscitation Algorithm–2015 Update.

Key Words: infant, newborn ■ infant, premature ■ oxygen ■ resuscitation

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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This 2019 focused update to the American Heart Association (AHA) neonatal resuscitation guidelines is based on the systematic review of initial oxygen concentration for term neonatal resuscitation[1] and initial oxygen concentration for preterm neonatal resuscitation[2] and the resulting "2019 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations" (CoSTR) from the International Liaison Committee on Resuscitation (ILCOR) Neonatal Life Support Task Force.[3–5]

The neonatal life support CoSTR drafts were posted online for public comment in January 2019.[3,4] In addition, the Neonatal Life Support Task Force has an expanded international committee of experts who collaborate to enrich these recommendations with a broader debate and vision. This committee meets in person twice a year. A summary containing the final wording of the 2 CoSTR documents has been published simultaneously with this focused update.[5]

AHA guidelines for cardiopulmonary resuscitation and emergency cardiovascular care are developed in concert with the ILCOR systematic review process. In 2015, the 5-year ILCOR evidence evaluation cycle transitioned to a continuous one, with systematic reviews performed as newly published evidence warrants or when the ILCOR Neonatal Life Support Task Force prioritizes a topic. The AHA writing group then reviews the evidence and updates the AHA guidelines as needed, typically on an annual basis. A description of the evidence review process is available in the 2017 CoSTR summary.[6] The ILCOR systematic review process uses the Grading of Recommendations Assessment, Development, and Evaluation methodology[7] and its associated nomenclature to determine the certainty of evidence and strength of recommendations for the CoSTR.

The AHA writing group for this 2019 focused update to the neonatal life support guidelines reviewed the studies and analyses of the 2018 ILCOR systematic reviews[1,2] and carefully considered the 2019 ILCOR Neonatal Task Force CoSTR[5] in the context of North American systems of care, levels of resource availability, and varied providers who follow AHA guidelines. In addition, the AHA writing group determined the Classes of Recommendation and Levels of Evidence according to the recommendations of the American College of Cardiology/AHA Task Force on Clinical Practice Guidelines[8] (Table) by using the process detailed in the "2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[9]

BACKGROUND

Although hypoxia and ischemia can injure multiple organs, adverse biochemical and physiologic outcomes also may result from even brief exposure to excessive oxygen during and after resuscitation.[10] In addition, preterm neonates are more susceptible than term neonates to clinical morbidities related to excessive oxygen exposure such as bronchopulmonary dysplasia, retinopathy of prematurity, and other important outcomes considered in the evidence review.[11,12] Consequently, separate CoSTRs were developed for term and late-preterm (≥35 weeks of gestation) newborns and for preterm (<35 weeks of gestation) newborns, reflecting differing indications for resuscitation, types of interventions, and outcomes of interest.[3,4]

The question of which initial oxygen concentration to use during resuscitation of term neonates was last reviewed by ILCOR in 2010.[13] The original AHA guidelines for oxygen use during neonatal resuscitation[14] were based on expert opinion and common practice and recommended the use of 100% oxygen for all newborns receiving respiratory support. Subsequent evidence from both animal and human studies has led to modifications of these recommendations. In 1998, the World Health Organization recommended 21% oxygen for basic newborn resuscitation when supplementary oxygen was not available.[15] Studies of normal transition after birth led to a recommendation that blended oxygen be titrated to achieve an oxygen saturation that is reflective of that observed in healthy babies born at term (ie, targeted saturation).[16,17] On the basis of studies that showed a lack of benefit of 100% oxygen for short-term respiratory outcomes and a decrease in mortality for term infants resuscitated with 21% oxygen, the ILCOR 2010 CoSTR[13] and AHA neonatal resuscitation guidelines[18] recommended the use of 21% oxygen to initiate positive-pressure ventilation for term infants.

The question of which initial oxygen concentration to use during the resuscitation of preterm neonates was last reviewed by ILCOR in 2015.[19] Most studies of preterm infants available at that time compared the use of high (60% to 100%) and low (21% to 30%) oxygen concentration and found no benefit from the use of high oxygen concentration for any of the outcomes of interest. This resulted in a recommendation for initiating resuscitation of preterm infants with a low oxygen concentration, as well as a specific recommendation against initiating resuscitation of preterm infants with high oxygen concentrations.[20] These recommendations reflected the value placed by the Neonatal Task Force on not exposing preterm infants to additional oxygen without proven benefit for critical or important outcomes.

The 2018 ILCOR systematic reviews addressed the use of lower initial oxygen concentrations compared with higher initial oxygen concentrations in both term[1] and preterm[2] neonatal resuscitation by using the Grading of Recommendations Assessment, Development, and Evaluation evidence evaluation methodology.[7]

INITIAL OXYGEN CONCENTRATION: TERM AND LATE-PRETERM NEWBORNS (≥35 WEEKS OF GESTATION)

Evidence Summary—Updated 2019

The 2018 ILCOR systematic review[1] compared the outcomes of term and

Table Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated August 2015)*

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS 1 (STRONG)	**Benefit >>> Risk**
Suggested phrases for writing recommendations: • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	
CLASS 2a (MODERATE)	**Benefit >> Risk**
Suggested phrases for writing recommendations: • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	
CLASS 2b (WEAK)	**Benefit ≥ Risk**
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	
CLASS 3: No Benefit (MODERATE) **(Generally, LOE A or B use only)**	**Benefit = Risk**
Suggested phrases for writing recommendations: • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	
Class 3: Harm (STRONG)	**Risk > Benefit**
Suggested phrases for writing recommendations: • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

late-preterm newborns (≥35 weeks of gestation) who received respiratory support after birth that used either 21% or 100% oxygen because no identified studies evaluated intermediate concentrations (between 22% and 99%, inclusive). The complete review included 10 original studies and 2 follow-up studies involving 2164 newborns. Three of the original studies were included only in sensitivity analyses because they were determined to have a critical risk of bias. In total, 7 randomized controlled trials (RCTs) and quasi-RCTs enrolling 1469 term and late-preterm newborns were included in the primary meta-analysis.[12,21–26]

All 7 included trials evaluated the outcome of short-term mortality, defined as mortality either in the hospital or within 30 days. In the meta-analysis, the summary relative risk (RR) of short-term mortality was lower in the 21% oxygen group (RR, 0.73 [95% CI, 0.57–0.94]).[1] This estimate was of low-level certainty because of the risk of bias and imprecision.

Two studies examined the outcome of neurodevelopmental impairment in survivors at 1 to 3 years of age.[25,27] The pooled estimate showed no statistically significant difference in risk between the 21% and 100% oxygen groups (RR, 1.41 [95% CI, 0.77–2.60]).[1] Five studies examined the outcome of hypoxic-ischemic encephalopathy,[21,22,24–26] defined as Sarnat stage 2 or 3.[28] Again, there was no statistically significant difference between the 21% and 100% oxygen groups (RR, 0.90 [95% CI, 0.71–1.14]).[1] No identified studies evaluated all-cause long-term mortality. Collectively, the studies were downgraded for risk of bias and imprecision and assigned as evidence of low certainty with respect to hypoxic-ischemic encephalopathy and very low certainty for long-term neurodevelopmental impairment.

Recommendations—Updated 2019

1. **In term and late-preterm newborns (≥35 weeks of gestation) receiving respiratory support at birth, the initial use of 21% oxygen is reasonable (Class 2a; Level of Evidence B-R).**

2. **One hundred percent oxygen should not be used to initiate resuscitation because it is associated with excess mortality (Class 3: Harm; Level of Evidence B-R).**

The current recommendations affirm the 2010[18] and 2015 AHA guidelines[20] and extend the recommendation against starting ventilation with 100% oxygen to term and late-preterm newborns. This is based on the large undesirable effect on short-term mortality associated with high initial oxygen concentration and the value attached to this outcome by parents and clinicians. Ambient air (21% oxygen) is available in all low- and well-resourced settings. Despite the lack of published economic analyses, there is likely to be greater feasibility and lower cost when resuscitation is initiated without added oxygen. Although evidence is still lacking on titration to achieve oxygen saturation targets, the use of preductal oxygen saturation targeting approximating the interquartile range measured in healthy term infants after vaginal birth at sea level is consistent with the high value placed on avoiding excessive oxygen exposure.

DISCUSSION

The 2010[18] and 2015 AHA guidelines for neonatal resuscitation[20] supported the initial use of 21% oxygen with subsequent supplementary oxygen use guided by target oxygen saturations measured by pulse oximetry in term and late-preterm newborns. At the time, these guidelines represented a departure from the decades-long use of 100% oxygen for all newborns receiving respiratory support. The guidelines were informed by 2 systematic reviews with meta-analyses.[29,30] The pooled estimates from these reviews reported lower mortality, fewer infants with time to first breath >3 minutes, and fewer infants with Apgar scores <7 at 5 minutes when 21% compared with 100% oxygen was used for initial mask ventilation. All studies included in these reviews were conducted >10 years ago, when pulse oximetry and oxygen titration were not routine. It remains unclear whether low versus high initial oxygen concentration will have the same result with oxygen titration as a cointervention.

The 2018 ILCOR systematic review and meta-analysis involved 1469 neonates ≥35 weeks of gestation enrolled in 7 randomized and quasi-randomized studies and reported a 27% relative survival benefit and a 4.6% absolute survival benefit (short-term) when 21% oxygen was compared with 100% oxygen for initial mask ventilation.[1] These benefits corresponded to 1 additional survivor (short-term) for 22 infants receiving 21% oxygen instead of 100% oxygen at birth. The Grading of Recommendations Assessment, Development, and Evaluation certainty of evidence was low for short-term mortality and hypoxic-ischemic encephalopathy and very low for long-term neurodevelopmental impairment. Furthermore, no studies were identified for the outcome of all-cause long-term mortality. All included studies compared 21% with 100% initial oxygen concentration. No studies were identified that compared intermediate oxygen concentrations, and no studies compared oxygen concentrations used during chest compressions.

The 2018 ILCOR systematic review and meta-analysis[1] confirmed a significant reduction in the critically important outcome of short-term mortality, without statistically significant differences in short- and long-term neurologic outcomes, with the use of initial 21% oxygen compared with 100% oxygen for term and late-preterm newborns (≥35 weeks of gestation) receiving respiratory support at birth. The authors estimated that 46 of 1000 fewer babies died when respiratory support at birth was started with 21% compared with 100% oxygen (95% CI, 73/1000 fewer–10/1000 fewer). As a result, the previous recommendations in the 2010 and 2015 AHA guidelines[18,20] are affirmed and extended to recommend against starting ventilation with 100% oxygen.

INITIAL OXYGEN CONCENTRATION: PRETERM NEWBORNS (<35 WEEKS OF GESTATION)

Evidence Summary—Updated 2019

The 2018 ILCOR systematic review compared several outcomes of preterm newborns (<35 weeks of gestation) who received respiratory support immediately after birth with

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
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Vishal S. Kapadia	UT Southwestern	NIH (PI for a clinical trial)*	None	None	None	None	None	None
Henry C. Lee	Stanford University	NIH (PI on a grant to implement in situ simulation training for neonatal resuscitation)*	None	None	None	None	None	None
Susan Niermeyer	University of Colorado	None	None	None	None	None	None	None
Georg M. Schmölzer	NA	NIH (R01, co-PI for premature infants receiving milking or delayed cord clamping, RCT)*; CIHR (PI for the SURV1VE Trial RCT [2 different chest compression techniques in newborn infants])*; HFSC (PI for grant to examine chest compression in a piglet model)*; SickKids Foundation and CIHR (PI to examine chest compression in piglets)*; NHMRC grant for delivery room resuscitation in near-term lambs (co-PI)*	None	None	None	None	None	None
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Gary M. Weiner	University of Michigan	None	None	None	None	None	None	None
Myra H. Wyckoff	UT Southwestern	None	None	None	None	None	None	None
Nicole K. Yamada	Stanford University	AHRQ (PI on the effects of standardized communication on team performance during neonatal resuscitation)†; NICHD (collaborator on a grant investigating the implementation of in situ simulation to improve delivery room outcomes in the California Perinatal Quality Care Collaborative)*	None	None	None	None	None	None
Jeanette G. Zaichkin	Self-employed	None	None	None	HeplerBroom LLC*	None	American Academy of Pediatrics†	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-mo period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

the use of a low initial oxygen concentration (≤50%) compared with a high initial oxygen concentration (>50%).[2] The reviewers identified 16 eligible studies enrolling 5697 newborns, including 10 RCTs,[11,31–39] 2 follow-up studies,[40,41] and 4 observational cohort studies.[42–45] Low initial oxygen was defined as 21% in 5 RCTs,[31,33,34,36,39] 30% in 4 RCTs,[11,35,37,38] and 50% in 1 RCT.[32] Oxygen saturation targeting was a cointervention in 8 RCTs[11,33–39] and in all 4 cohort studies.[42–45] When oxygen saturation targeting was used, nearly all newborns randomized to initiate resuscitation with 21% oxygen required supplementary oxygen to achieve the specified target. Because oxygen saturation targeting resulted in rapid changes in inspired oxygen concentrations, the subjects enrolled in these trials were exposed to different oxygen concentrations for only the first 5 to 7 minutes of life.

The pooled estimate of 10 RCTs enrolling 968 preterm newborns showed no statistically significant difference in the outcome of all-cause short-term mortality (hospital discharge or 30 days) when respiratory support initiated with a lower oxygen concentration was compared with support initiated with a higher oxygen concentration (RR, 0.83 [95% CI, 0.50–1.37]).[2] In a subgroup analysis of 7 RCTs[11,33,34,36–39] enrolling 467 newborns ≤28 weeks of gestation, there was no significant difference in short-term mortality (RR, 0.92 [95% CI, 0.42–1.94]).[2]

Similarly, the ILCOR systematic review found no differences in any of the prespecified secondary outcomes, including long-term mortality, long-term neurodevelopmental impairment, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, or major (grade III or IV) intraventricular hemorrhage.[2] White matter injury of prematurity was not included as a secondary outcome. Additional subgroup analyses that assessed the effect of varying the definition of low and high oxygen concentration, the risk of bias, and the use of oxygen saturation targeting as a cointervention found no differences in primary or secondary outcomes. When data from 2 observational cohort studies were pooled,[44,45] initiating resuscitation with lower oxygen was associated with a statistically significant benefit in long-term mortality for all preterm newborns and the subgroup of newborns ≤28 weeks of gestation.[2]

Most of the studies included in the ILCOR systematic review were judged to have an unclear risk of bias because of imprecision, inconsistency, and lack of blinding of interventions and outcomes.[2] As a result of the unclear risk of bias and the small number of very preterm newborns enrolled in the randomized trials, there was very low certainty for all outcome estimates, and the benefit or harm from initiating positive-pressure ventilation with low compared with high oxygen concentrations remains inconclusive. Large randomized trials enrolling very preterm newborns are needed to achieve the optimal information size. Furthermore, scant evidence exists on the use of intermediate oxygen concentrations (30% to 60%).

Recommendation—Updated 2019

1. **In preterm newborns (<35 weeks of gestation) receiving respiratory support at birth, it may be reasonable to begin with 21% to 30% oxygen with subsequent oxygen titration based on pulse oximetry (Class 2b; Level of Evidence C-LD).**

The current recommendation remains consistent with the 2015 AHA guidelines update.[20] Given that nearly all trials included in the 2018 ILCOR review defined low initial oxygen as 21% to 30% oxygen,[2] the current recommendation suggests this as a reasonable initial oxygen concentration. In this recommendation, high value is placed on avoiding additional oxygen exposure without evidence of benefit for critical or important outcomes. The writing group acknowledges that

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
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Roberta L. Keller	University of California, San Francisco	None	None	None	None	None	None	None
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Janet Soul	Boston Children's Hospital	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-mo period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

although the evidence identified in the 2018 ILCOR review was weak and uncertain, it also showed no statistically significant difference in outcomes when low versus high initial oxygen concentration was chosen for preterm resuscitation at birth. In the absence of a new evidence review for subsequent oxygen titration, it remains prudent to continue to titrate oxygen concentrations to achieve preductal oxygen saturation approximating the interquartile range measured in healthy term infants after vaginal birth at sea level, as recommended in the 2015 AHA guidelines update.[20]

Discussion

The 2015 AHA guidelines update for neonatal resuscitation recommended that resuscitation of preterm newborns <35 weeks of gestation should be initiated with low oxygen (21% to 30%) and that the oxygen concentration should be titrated to achieve a preductal oxygen saturation approximating the interquartile range measured in healthy term infants after vaginal birth at sea level.[20]

Since the release of the 2015 guidelines, new data have been published on the initial oxygen concentration used in the delivery room for preterm infants (<35 weeks of gestation), prompting the ILCOR Neonatal Life Support Task Force to complete a new systematic review of the available evidence.[2] Of particular concern was the recent publication of the To2rpido RCT (Targeted Oxygen in the Resuscitation of Preterm Infants and Their Developmental Outcomes).[39] In a subgroup analysis of preterm infants <28 weeks of gestation, the To2rpido investigators reported that the use of 21% oxygen for initial positive-pressure ventilation, compared with 100% oxygen, increased the risk of death before hospital discharge (RR, 3.9 [95% CI, 1.1–13.4]).[39] However, the ILCOR systematic review identified significant concerns about the risk of bias in this study, including very limited enrollment, early study termination, lack of investigator equipoise, use of an unblinded intervention, and increased risk seen only in a post hoc subgroup analysis.[2] Because the review and meta-analysis found no difference in any primary or secondary outcomes with the To2rpido trial included, the recommendation that resuscitation of preterm newborns should begin with low oxygen with subsequent titration to meet goal saturations remains unchanged. This reflects a continued preference to avoid exposing preterm newborns to additional oxygen without evidence demonstrating a benefit for critical or important outcomes. Important knowledge gaps remain in the understanding of oxygen use for positive-pressure ventilation among term, late-preterm, and preterm newborns after birth. Additional research is needed to evaluate the role of intermediate oxygen concentrations for the initiation of positive-pressure ventilation and to define the most appropriate oxygen saturation targets. Many subpopulations of newborns (eg, newborns with congenital heart disease and other malformations) have not been adequately studied, and many outcomes (eg, white matter injury of prematurity) have not been fully assessed. These newborns and their outcomes may be affected by either hypoxemia or hyperoxemia. Until reliable data on a specific population or outcome are available, the consistent and practical educational approach will be to manage them according to the guidelines for the wider population of preterm and term newborns requiring resuscitation.

SUMMARY

This review of the initial use of oxygen in newborns receiving respiratory support at birth remains consistent with the 2015 AHA neonatal resuscitation guidelines.[20] In term and late-preterm newborns (≥35 weeks of gestation), the initial use of 21% oxygen is reasonable (*Class 2a; Level of Evidence B-R*). In term and late-preterm newborns, the initial use of 100% oxygen is not recommended (*Class 3: Harm; Level of Evidence B-R*).

In preterm newborns (<35 weeks of gestation), starting with 21% to 30% oxygen with subsequent targeted titration of supplementary oxygen may be reasonable (*Class 2b; Level of Evidence C-LD*). These guidelines do not alter the Neonatal Resuscitation Algorithm–2015 Update.[19,20]

Knowledge gaps for term, late-preterm, and preterm newborn resuscitation include the following: (1) uncertainty about the impact of changes in umbilical cord management; (2) uncertainty about the impact of changes in oxygen saturation monitoring and targeted titration of inspired oxygen; (3) uncertainty about the effects of intermediate initial inspired oxygen concentrations; (4) uncertainty about whether a single initial oxygen concentration is optimal for newborns with varying pathology or conditions such as antenatal fetal distress at any given gestational age; and (5) uncertainty about the impact of lower initial oxygen use on neurodevelopmental outcomes in preterm newborns. With so many unanswered questions, it is expected that future scientific evidence will provide new insights, and guideline updates will be required.

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2019 American Heart Association Focused Update on Neonatal Resuscitation: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Marilyn B. Escobedo, Khalid Aziz, Vishal S. Kapadia, Henry C. Lee, Susan Niermeyer, Georg M. Schmölzer, Edgardo Szyld, Gary M. Weiner, Myra H. Wyckoff, Nicole K. Yamada and Jeanette G. Zaichkin

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2019 American Heart Association Focused Update on Pediatric Basic Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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abstract

This 2019 focused update to the American Heart Association pediatric basic life support guidelines follows the 2019 systematic review of the effects of dispatcher-assisted cardiopulmonary resuscitation (DA-CPR) on survival of infants and children with out-of-hospital cardiac arrest. This systematic review and the primary studies identified were analyzed by the Pediatric Task Force of the International Liaison Committee on Resuscitation. It aligns with the International Liaison Committee on Resuscitation's continuous evidence review process, with updates published when the International Liaison Committee on Resuscitation completes a literature review based on new published evidence. This update summarizes the available pediatric evidence supporting DA-CPR and provides treatment recommendations for DA-CPR for pediatric out-of-hospital cardiac arrest. Four new pediatric studies were reviewed. A systematic review of this data identified the association of a significant improvement in the rates of bystander CPR and in survival 1 month after cardiac arrest with DA-CPR. The writing group recommends that emergency medical dispatch centers offer DA-CPR for presumed pediatric cardiac arrest, especially when no bystander CPR is in progress. No recommendation could be made for or against DA-CPR instructions when bystander CPR is already in progress.

Keywords: cardiopulmonary resuscitation ■ children ■ emergency medical dispatcher ■ heart arrest ■ pediatrics

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This 2019 focused update to the American Heart Association (AHA) pediatric basic life support (PBLS) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care is based on the systematic review of dispatcher instruction in CPR (pediatrics)[1] and the resulting Consensus on Science With Treatment Recommendations (CoSTR) from the Pediatric Task Force of the International Liaison Committee on Resuscitation (ILCOR). A draft pediatric CoSTR was posted online for public comment,[2] and a summary document containing the final CoSTR wording has

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Jonathan P. Duff	University of Alberta and Stollery Children's Hospital (Canada)	None	None	None	None	None	None	None
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S. Jill Ley	American Association of Critical Care Nurses	None	None	None	None	None	None	None
Tia T. Raymond	Medical City Children's Hospital	NIH R01 (OPTI-VENT [Optimized and Personalized Ventilation to Improve Pediatric Cardiac Arrest Outcomes], Studies in Neonatal and Pediatric Resuscitation)*; NIH R03 (The Impact on Outcomes of Emergency Medications at the Bedside in Pediatric Cardiac ICU Patients)*	None	None	None	None	None	None
Robert Michael Sutton	The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine	NHLBI (PI on CPR Quality Improvement trial)*	None	None	Roberts and Durkee†; Lowis and Gellen*; Donahue, Durham, and Noonan*	None	None	None
Alexis A. Topjian	The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine	NIH (subaward)*	None	None	Plaintiff*	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-mo period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

* Significant.

Reviewer Disclosures

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This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-mo period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.
* Significant.

been published simultaneously with this document.[3]

AHA guidelines and focused updates are developed in concert with ILCOR's systematic review process. In 2015, the ILCOR evidence evaluation process and the AHA development of guidelines and focused updates transitioned to a continuous, simultaneous process, with systematic reviews performed as new published evidence warrants or when the ILCOR Pediatric Task Force prioritizes a topic. The AHA science experts review new evidence and update the AHA PBLS guidelines as needed, typically on an annual basis. A description of the evidence review process is available in the "2017 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations Summary."[4]

The ILCOR systematic review process uses the Grading of Recommendations Assessment, Development, and Evaluation methodology and its associated nomenclature to determine strength of recommendation and certainty of evidence for the CoSTR. The expert writing group for this 2019 PBLS focused update reviewed the studies and analysis of the 2019 ILCOR CoSTR summary[1,3] and carefully considered the ILCOR Pediatric Task Force consensus recommendations in light of the structure and resources of the out-of-hospital and in-hospital resuscitation systems and providers who use AHA guidelines. In addition, the writing group came to consensus regarding the Classes of Recommendation and Levels of Evidence according to the nomenclature developed by the American College of Cardiology/AHA recommendations for developing clinical practice guidelines (Table 1)[5] by using the process detailed in the "2015 AHA Guidelines Update for

Table 1 Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated August 2015)*

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
CLASS 1 (STRONG) — **Benefit >>> Risk** **Suggested phrases for writing recommendations:** • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	**LEVEL A** • High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
CLASS 2a (MODERATE) — **Benefit >> Risk** **Suggested phrases for writing recommendations:** • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	**LEVEL B-R** — **(Randomized)** • Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
CLASS 2b (WEAK) — **Benefit ≥ Risk** **Suggested phrases for writing recommendations:** • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	**LEVEL B-NR** — **(Nonrandomized)** • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies
CLASS 3: No Benefit (MODERATE) (Generally, LOE A or B use only) — **Benefit = Risk** **Suggested phrases for writing recommendations:** • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	**LEVEL C-LD** — **(Limited Data)** • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects
Class 3: Harm (STRONG) — **Risk > Benefit** **Suggested phrases for writing recommendations:** • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	**LEVEL C-EO** — **(Expert Opinion)** • Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[6]

It is important to note that this 2019 PBLS focused update evaluates only the recommendations for the use of dispatcher-assisted CPR (DA-CPR) in pediatric out-of-hospital cardiac arrest (OHCA). All other recommendations and algorithms published in the 2017 focused update,[7] "Part 11: Pediatric Basic Life Support and Cardiopulmonary Resuscitation Quality" of the 2015 guidelines update,[8] and "Part 13: Pediatric Basic Life Support" of the "2010 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care"[9] remain the official recommendations of the AHA Emergency Cardiovascular Care Science Subcommittee and writing groups.

DISPATCHER INSTRUCTION IN CPR

Effective bystander CPR is a key component of the chain of survival from OHCA.[10,11] Unfortunately, rates of bystander CPR remain low for both adults[12] and children[11–13] with OHCA. In adults with OHCA, the provision of

Table 2 Summary of Pediatric Studies on DA-CPR

Author	Country	Sample Size, n	Study Duration	Design	Primary Outcomes
Goto et al,[11] 2014	Japan	5009	January 2008–December 2010	Prospective cohort	Survival and favorable neurologic outcome at 1 mo
Akahane et al,[16] 2012	Japan	1780	January 2005–December 2008	Prospective cohort	Survival and favorable neurologic outcome at 1 mo
Chang et al,[13] 2018	Korea	1953	January 2012–December 2016	Cross-sectional	Survival and favorable neurologic outcome at hospital discharge
Lee et al,[18] 2019	Korea	1013	January 2012–December 2013	Cross-sectional	Survival and favorable neurologic outcome at hospital discharge
Ro et al,[17] 2016	Korea	1529	January 2012–December 2014	Cross-sectional	Survival and favorable neurologic outcome at hospital discharge

DA-CPR indicates dispatch-assisted cardiopulmonary resuscitation.
Modified from Nikolaou et al[1] with permission. Copyright © 2019, Elsevier.

CPR instructions by emergency dispatchers has been associated with increased rates of bystander CPR and improved patient outcomes.[1,14,15] However, bystander CPR rates for pediatric OHCA remain low, even when DA-CPR is offered.[16,17]

A variety of terms have been used to identify the personnel at an emergency telephone call center who are charged with answering the call, interacting with the caller, and assigning the needed care providers to the incident scene (traditionally called *dispatchers*). Terminology is similarly varied for the process the dispatcher uses to provide real-time CPR instructions to bystanders at the scene of an OHCA. In this PBLS focused update, to remain consistent with the ILCOR evidence review, the term *DA-CPR* will be used to describe such coaching, recognizing that other terms (such as *telecommunicator CPR* and *telephone CPR*) could be substituted.

EVIDENCE SUMMARY—UPDATED 2019

There has been no previous review focusing specifically on the effect of DA-CPR instructions for pediatric OHCA, although the 2017 PBLS focused update[7] included registry data from systems that provided such instructions. The systematic review analyzed both adult and pediatric data (Table 2).[1] The ILCOR Pediatric Task Force and the AHA writing group reviewed the pediatric studies included in that systematic review that compared outcomes for patients who were offered DA-CPR.[11,13,16,19] Patients in a study from Korea[18] were not evaluated separately in the ILCOR review because they were included in another larger study from the same registry[13] involving overlapping years; in addition, the smaller study[18] did not compare patients offered DA-CPR with those not offered DA-CPR. Both adjusted and unadjusted study outcomes of the remaining studies were analyzed, with the caution that unadjusted outcomes could be confounded by several factors such as cause of arrest, location of arrest, changes in resuscitation guidelines over time, and differences in emergency medical services (EMS) protocols.[1]

An observational study from the All-Japan Utstein Registry reported the association of DA-CPR with increased survival at 1 month in 1780 children with OHCA enrolled between January 2005 and December 2008.[16] Results were adjusted for age, sex, bystander type, cause of cardiac arrest, and interval between the call to EMS and arrival. DA-CPR was offered in 28.4% of patients. Bystander CPR was performed for more than two-thirds (68.7%, 347 of 505) of patients when callers were offered DA-CPR but was performed for only 27.8% (354 of 1275) of patients when callers were not offered DA-CPR; thus, DA-CPR was associated with an almost 3-fold increase in the likelihood of bystander CPR, a known contributor to survival. DA-CPR offered by dispatchers was significantly associated with improved 1-month survival (odds ratio [OR], 1.46 [95% CI, 1.05–2.03]) but not with 1-month favorable neurologic outcome.[16]

In a later study from the same All-Japan Utstein Registry, Goto and colleagues[11] examined the effect of DA-CPR on favorable 1-month neurologic outcome and survival to 1 month in 5009 children with OHCA enrolled from 2008 through 2010. It is important to note that the patients with callers who were offered DA-CPR were younger (ie, infants) and more likely to have an unwitnessed arrest, a presumed cardiac cause of the arrest, and bystander CPR compared with those who were not offered DA-CPR. Outcomes were adjusted for age, sex, presumed cardiac cause, initial rhythm, witnessed versus nonwitnessed arrest, and call-to-response interval. Callers for 2698 patients (53.9%) were offered DA-CPR; of these, 2019 patients (74.8%) actually received bystander CPR. The bystander CPR consisted of chest compression–only CPR for 54.5% (1101 of 2019), conventional CPR for 42.3% (855 of 2019), and rescue breaths only for 3.0% (63 of 2019). Offered DA-CPR was significantly associated with 1-month survival (adjusted OR, 1.43 [95% CI, 1.14–1.79]) but not with 1-month favorable neurologic outcome. The provision of bystander CPR, with or without dispatcher instruction, was associated with improved odds of survival and survival with favorable neurologic outcomes compared with no bystander CPR.[11]

The first of 2 Korean registry studies examined the association of bystander CPR, with and without dispatcher assistance, with survival to hospital discharge of children with OHCA between 2012 and 2014.[17] Data were adjusted for age, sex, location, cause of the arrest, witnessed or unwitnessed arrest, initial rhythm, and EMS response interval. Of 1529 patients, 502 (32.8%) had DA-CPR, 264 (17.3%) had bystander CPR provided without dispatcher assistance, and 763 (49.9%) had no bystander CPR provided. After multivariable analysis, both DA-CPR (OR, 2.14 [95% CI, 1.01–4.58]) and unassisted bystander CPR (adjusted OR, 3.52 [95% CI, 1.56–7.92]) were associated with increased likelihood of favorable neurologic outcome at hospital discharge compared with no bystander CPR. When analyzed by patient age, survival in children 9 to 18 years of age more than doubled if the child received bystander CPR with or without dispatcher assistance. Children between 1 and 8 years of age had improved outcomes with unassisted bystander CPR but not with DA-CPR. In infants (<12 months of age), there was no difference in outcome between the bystander CPR and no bystander CPR groups.[17]

In a more recent study (between 2012 and 2015) of 2020 children with OHCA from the same Korean database, Chang and colleagues[13] examined the association of DA-CPR with survival to hospital discharge. They again noted the association of bystander CPR (versus no bystander CPR) with more than double the survival with favorable neurologic function at hospital discharge, whether that bystander CPR was delivered with or without dispatcher assistance.

In the analysis of these 4 pediatric studies performed in the systematic review,[1] offering DA-CPR was not associated with significantly improved 1-month favorable neurologic outcome but was associated with improved 1-month survival (OR, 1.46 [95% CI, 1.05–2.03]).[11] DA-CPR was also associated with significantly increased likelihood of bystander CPR and shortened time from arrest to delivery of CPR. For those patients who actually received bystander CPR, DA-CPR was associated with improved survival with favorable neurologic outcome at 1 month compared with no bystander CPR (adjusted OR, 1.81 [95% CI, 1.23–2.67]).[11] However, as noted, patients in this large Japanese study who were offered DA-CPR were more likely to be infants, to have a presumed cardiac cause of arrest, and to have an unwitnessed arrest compared with those who were not offered DA-CPR. It is notable that the outcome of patients who received bystander DA-CPR was associated with a lower likelihood of favorable neurologic outcome at 1 month after arrest (OR, 0.57 [95%, CI, 0.39–0.84]) compared with patients who received unassisted bystander CPR.

2019 RECOMMENDATIONS—NEW

There is no previous recommendation on this topic.

1. **We recommend that emergency medical dispatch centers offer DA-CPR instructions for presumed pediatric cardiac arrest (Class 1; Level of Evidence C-LD).order**

2. **We recommend that emergency dispatchers provide CPR instructions for pediatric cardiac arrest when no bystander CPR is in progress (Class 1; Level of Evidence C-LD).**

There is insufficient evidence to make a recommendation for or against DA-CPR instructions for pediatric cardiac arrest when bystander CPR is already in progress.

DISCUSSION

In making these recommendations, the writing group considered a number of factors influencing potential effectiveness of DA-CPR and bystander actions. Although the level and quality of evidence for DA-CPR in pediatric OHCA are low, we agreed with the ILCOR Pediatric Task Force that the likelihood of benefit from DA-CPR clearly outweighs the risk. Higher 1-month postarrest survival is associated with offered DA-CPR compared with arrests when DA-CPR was not offered.[11] In addition, there is an association with increased likelihood of secondary outcomes such as likelihood of bystander CPR and reduced time to CPR among systems offering DA-CPR.[1] The key point of these studies is that DA-CPR is associated with increased survival and the likelihood of bystander CPR. Bystander CPR, with or without dispatcher assistance, was associated with improved survival with favorable neurologic outcome at hospital discharge[13] and at 1 month[11] compared with no CPR.

There is clear evidence that bystander CPR is an important positive prognostic factor in pediatric OHCA, and EMS systems that offer DA-CPR document higher bystander CPR rates. However, bystander CPR rates in pediatric OHCA, even with dispatcher assistance, remain low. More work needs to be done to improve bystander CPR rates for adults and children.[20–22]

The available evidence does not clarify the effect of the provision of DA-CPR when bystander CPR is already in progress. As noted, there is some low-quality (ie, observational/registry rather than randomized) evidence of an association between offering DA-CPR when bystander CPR is already in progress and worse 1-month neurologic outcomes in

pediatric patients with cardiac arrest. More research is needed to identify the reasons for this finding. It is possible that most bystanders who begin CPR independently (ie, even before dispatcher instructions are offered) are trained and may be proficient in CPR, so the CPR provided may be of higher quality than that delivered by an untrained bystander after dispatcher instructions. The writing group weighed the association of potential harm (ie, worse 1-month neurologic outcomes) with offering DA-CPR when bystander CPR was in progress, as well as the potential harm that could result by failing to offer DA-CPR when needed, and determined that there was insufficient evidence to support a recommendation at this time.

The writing group also recognizes that the data for this recommendation come from registry data from 2 very different EMS systems (Korea and Japan). Differences in how these EMS systems function may confound more global recommendations.

This review did not examine the content of the CPR instructions provided by dispatchers delivering DA-CPR. In the pediatric studies reviewed, the instructions provided by the dispatcher varied according to presumed bystander CPR skill level, cause of the arrest, and the patient's age. Only 1 study systematically examined the effects of the method of CPR suggested by dispatchers, with an improvement in favorable neurologic outcome at 1 month associated with conventional CPR versus chest compression–only CPR.[11] Current AHA PBLS guidelines recommend that conventional CPR be provided for infants and children in cardiac arrest.[7] The current guidelines also recommend that if rescuers are unable or unwilling to provide rescue breaths for pediatric arrest, then they should provide compression-only CPR. Given the importance of conventional CPR in pediatric cardiac arrest, more research is needed to determine the quality and content of dispatcher-assisted conventional CPR and the outcomes of patients receiving dispatcher-assisted conventional CPR compared with dispatcher-assisted chest compression–only CPR. Finally, additional research is needed to determine if and when dispatchers should offer CPR instructions when bystander CPR is already in progress.

The American Heart Association and the American Academy of Pediatrics make every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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2019 American Heart Association Focused Update on Pediatric Basic Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Jonathan P. Duff, Alexis A. Topjian, Marc D. Berg, Melissa Chan, Sarah E. Haskell, Benny L. Joyner Jr, Javier J. Lasa, S. Jill Ley, Tia T. Raymond, Robert Michael Sutton, Mary Fran Hazinski and Dianne L. Atkins

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2019 American Heart Association Focused Update on Pediatric Advanced Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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abstract

This 2019 focused update to the American Heart Association pediatric advanced life support guidelines follows the 2018 and 2019 systematic reviews performed by the Pediatric Life Support Task Force of the International Liaison Committee on Resuscitation. It aligns with the continuous evidence review process of the International Liaison Committee on Resuscitation, with updates published when the International Liaison Committee on Resuscitation completes a literature review based on new published evidence. This update provides the evidence review and treatment recommendations for advanced airway management in pediatric cardiac arrest, extracorporeal cardiopulmonary resuscitation in pediatric cardiac arrest, and pediatric targeted temperature management during post–cardiac arrest care. The writing group analyzed the systematic reviews and the original research published for each of these topics. For airway management, the writing group concluded that it is reasonable to continue bag-mask ventilation (versus attempting an advanced airway such as endotracheal intubation) in patients with out-of-hospital cardiac arrest. When extracorporeal membrane oxygenation protocols and teams are readily available, extracorporeal cardiopulmonary resuscitation should be considered for patients with cardiac diagnoses and in-hospital cardiac arrest. Finally, it is reasonable to use targeted temperature management of 32°C to 34°C followed by 36°C to 37.5°C, or to use targeted temperature management of 36°C to 37.5°C, for pediatric patients who remain comatose after resuscitation from out-of-hospital cardiac arrest or in-hospital cardiac arrest.

Key Words: advanced cardiac life support ■ airway management ■ cardiopulmonary resuscitation ■ extracorporeal membrane oxygenation ■ heart arrest ■ hypothermia, induced ■ pediatrics

The American Heart Association and the American Academy of Pediatrics make every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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This 2019 focused update to the American Heart Association (AHA) pediatric advanced life support (PALS) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) is based on 3 systematic reviews[1–3] and the resulting "2019 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations" (CoSTR) from the Pediatric Life Support Task Force of the International Liaison Committee

on Resuscitation (ILCOR).[4] This pediatric life support task force CoSTR addressed 3 topics: advanced airway management in pediatric cardiac arrest, extracorporeal CPR (ECPR) in pediatric cardiac arrest, and pediatric targeted temperature management (TTM) during post–cardiac arrest care. The draft pediatric CoSTRs were posted online for public comment,[5–7] and a summary document containing the final CoSTR wording has been published simultaneously with this focused update.[4]

AHA guidelines for CPR and ECC are developed in concert with ILCOR's systematic review process. In 2015, the ILCOR evidence evaluation process and the AHA development of guidelines updates transitioned to a continuous, simultaneous process, with systematic reviews performed as new published evidence warrants or when the ILCOR Pediatric Life Support Task Force prioritizes a topic. The AHA science experts review the new evidence and update the AHA's guidelines for CPR and ECC as needed, typically on an annual basis. A description of the evidence review process is available in the 2017 ILCOR summary.[8]

The ILCOR systematic review process uses the Grading of Recommendations Assessment, Development, and Evaluation methodology and its associated nomenclature to determine the strength of recommendation and certainty of effect for the CoSTR. The expert writing group for this 2019 PALS focused update analyzed and discussed the original studies and carefully considered the ILCOR Pediatric Life Support Task Force consensus recommendations[4] in light of the structure and resources of the out-of-hospital and in-hospital resuscitation systems and providers who use AHA guidelines. In addition, the writing group came to a consensus about the Classes of Recommendation and Levels of Evidence according to the nomenclature developed by the American College of Cardiology/AHA recommendations for developing clinical practice guidelines (Table)[9] by using the process detailed in the "2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[10]

It is importantto note that this 2019 focused update to the AHA PALS guidelines re-evaluates only the recommendations for the use of advanced airway management during cardiac arrest, the use of ECPR during cardiac arrest, and the use of TTM after cardiac arrest. All other recommendations and algorithms published in "Part 12: Pediatric Advanced Life Support" in the 2015 AHA guidelines update[11] and "Part 14: Pediatric Advanced Life Support" in the "2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care"[12] remain the official recommendations of the AHA ECC Science Subcommittee and writing groups. The other recommendations contained in the 2017 and 2018 focused updates to the AHA's pediatric basic and advanced life support guidelines continue to apply to care delivered to pediatric patients in cardiac arrest.[13,14]

ADVANCED AIRWAY INTERVENTIONS IN PEDIATRIC CARDIAC ARREST

Most pediatric cardiac arrests are triggered by respiratory deterioration.[15,16] As a result, airway management and ventilation management are fundamental components of PALS. A number of options exist for airway management in pediatric cardiac arrest. Although the majority of pediatric patients can be successfully ventilated with bag-mask ventilation (BMV), this method requires interruptions in chest compressions and is associated with risk of aspiration and barotrauma. Although endotracheal intubation can partially mitigate the risk of aspiration and enables delivery of uninterrupted chest compressions, it requires specialized equipment and skilled providers. Pediatric airway anatomy differs from that of adults, so tracheal intubation may be more difficult for healthcare professionals who do not routinely intubate pediatric patients. A supraglottic airway (SGA) such as the laryngeal mask airway may be easier to place than an endotracheal tube, but it does not provide a definitive airway and does not mitigate the risk of aspiration.

Evidence Summary—Updated 2019

The 2019 ILCOR Pediatric Life Support Task Force and the AHA pediatric writing group reviewed 14 studies of advanced airway interventions in pediatric patients with cardiac arrest. This included a clinical trial,[17] 3 propensity-adjusted studies,[18–20] 8 retrospective cohort studies,[21–28] and 2 retrospective studies.[29,30] The review included evidence for the use of an advanced airway (endotracheal intubation or SGA) versus BMV only.[4] This topic was last reviewed in 2010,[12] and the previous review did not directly compare outcomes associated with these 3 modalities.

Endotracheal Intubation Compared With BMV

All 14 studies in the systematic review examined the outcomes of endotracheal intubation versus BMV during pediatric cardiac arrest. The only clinical trial in the review randomized pediatric patients with out-of-hospital cardiac arrest (OHCA) to either BMV alone or BMV followed by endotracheal intubation.[17] There was no significant difference between the groups in favorable neurologic outcome or survival to hospital discharge.

Two propensity-adjusted studies were included in the review. In

a database study from the Get With The Guidelines–Resuscitation registry, endotracheal intubation during in-hospital cardiac arrest (IHCA) was associated with decreased survival to hospital discharge.[18] A review from an American cardiac arrest registry, CARES (American Cardiac Arrest Registry to Enhance Survival), of pediatric patients with OHCA comparing outcomes of patients treated with BMV and those treated with endotracheal intubation found an association between BMV and more than double the rate of survival to hospital discharge (odds ratio, 2.56 [95% CI, 1.69–3.85]).[19]

SGA Placement Compared With BMV Alone

Four observational studies were identified in the 2019 ILCOR systematic review of pediatric SGA versus BMV. All were focused on patients with OHCA. Two presented propensity-adjusted cohort data,[19,20] and 2 provided simple observational data.[26,28] In the 2 propensity-adjusted reviews, from the All-Japan Utstein Registry[20] and CARES,[19] comparing outcomes of SGA versus BMV, there was no association between the use of SGA and increased favorable neurologic outcome. In 2 non–propensity-matched observational studies comparing the use of SGA with BMV,[26,28] the SGA was associated with a significant increase in survival to hospital discharge and return of spontaneous circulation.

SGA Placement Compared With Endotracheal Intubation

Four observational studies (2 were propensity adjusted) also compared endotracheal intubation with SGA in pediatric patients with OHCA. When compared, neither SGA nor endotracheal intubation was associated with a significant increase or decrease in favorable neurologic outcome or survival to hospital discharge.[19,20,26,28] Similarly, when SGA and endotracheal intubation were compared, neither was associated with significant improvement in survival to hospital admission. However, 1 cohort study found improved survival associated with endotracheal intubation compared with SGA.[28]

Additional Considerations

The pediatric ILCOR CoSTR authors attempted to conduct a subgroup analysis to compare outcomes of pediatric IHCA and OHCA, as well as traumatic versus medical causes of arrest. Outcomes from IHCA and OHCA were similar. However, very few studies focused on IHCA; these included 1 propensity-matched cohort study[18] and 2 other cohort studies.[23,27] Outcomes of traumatic and nontraumatic arrest could not be compared because published studies included only a small number of patients identified as having traumatic arrest.

Recommendation—Updated 2019

1. **BMV is reasonable compared with advanced airway interventions (endotracheal intubation or SGA) in the management of children during cardiac arrest in the out-of-hospital setting (Class 2a; Level of Evidence C-LD)**.

We cannot make a recommendation for or against the use of an advanced airway for IHCA management. In addition, no recommendation can be made about which advanced airway intervention is superior in either OHCA or IHCA.

Discussion

The use of advanced airways in pediatric cardiac arrest was last reviewed by ILCOR in 2010, with the following recommendation: "In the prehospital setting it is reasonable to ventilate and oxygenate infants and children with a bag-mask device, especially if transport time is short (Class IIa, LOE [Level of Evidence] B)."[12] This 2019 focused update reaffirms the 2010 recommendation with no significant changes. In addition, we highlight the evidence associated with the use of specific types of airway intervention, endotracheal intubation and SGAs, comparing their effects with those of BMV. The evidence for this recommendation was largely from observational studies, so reported findings must be interpreted as associated with, rather than caused by, the intervention. However, the writing group agreed that a Class 2a recommendation was appropriate. When used by providers with proper experience and training, BMV was not associated with inferior outcomes compared with endotracheal intubation or SGA; thus, BMV is a reasonable alternative to these advanced airways, which may require more specific training or equipment. During OHCA, transport time, provider skill level and experience, and equipment availability should be considered in the selection of the most appropriate airway intervention. If BMV is ineffective despite appropriate optimization, more advanced airway interventions should be considered.

The writing group determined that there was insufficient evidence to make any recommendation about advanced airway management for IHCA and could not determine whether either endotracheal intubation or SGA was superior in either setting.

ECPR FOR IHCA

The use of extracorporeal membrane oxygenation (ECMO) as a form of mechanical circulatory rescue for failed conventional CPR (ie, ECPR) has gained popularity since its first use as a form of postcardiotomy rescue in children after surgery for congenital heart disease.[31,32] *ECPR* is defined as the rapid deployment of venoarterial ECMO during active CPR or for patients with intermittent

Table Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated August 2015)*

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
CLASS 1 (STRONG) — **Benefit >>> Risk** **Suggested phrases for writing recommendations:** • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	**LEVEL A** • High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
CLASS 2a (MODERATE) — **Benefit >> Risk** **Suggested phrases for writing recommendations:** • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	**LEVEL B-R** — **(Randomized)** • Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
CLASS 2b (WEAK) — **Benefit ≥ Risk** **Suggested phrases for writing recommendations:** • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	**LEVEL B-NR** — **(Nonrandomized)** • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies
CLASS 3: No Benefit (MODERATE) (Generally, LOE A or B use only) — **Benefit = Risk** **Suggested phrases for writing recommendations:** • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	**LEVEL C-LD** — **(Limited Data)** • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects
Class 3: Harm (STRONG) — **Risk > Benefit** **Suggested phrases for writing recommendations:** • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	**LEVEL C-EO** — **(Expert Opinion)** • Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

return of spontaneous circulation. ECPR is a resource-intense, complex multidisciplinary therapy that traditionally has been limited to large academic medical centers with providers who have expertise in the management of children with cardiac disease. Judicious use of ECPR for specialized patient populations and within dedicated and highly practiced environments has proved successful, especially for IHCA with reversible causes.[33] ECPR use rates have increased, with single-center reports in both adults and children suggesting that application of this therapy across broader patient populations may improve survival after both OHCA and IHCA.[34–36]

Evidence Summary—Updated 2019

The ILCOR Pediatric Life Support Task Force and the AHA pediatric writing group reviewed 3 studies on the use of ECPR in pediatric cardiac arrest. The first study was a retrospective review (2000–2008) of the Get With The Guidelines–Resuscitation registry of pediatric patients with IHCA after cardiac surgery.[37] On adjusted multivariate analysis, the use of ECPR was associated with higher rates of survival to hospital discharge than conventional CPR. A second review of the same database used a propensity

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Jonathan P. Duff	University of Alberta and Stollery Children's Hospital (Canada)	None	None	None	None	None	None	None
Dianne L. Atkins	University of Iowa	None	None	None	None	None	None	None
Marc D. Berg	Stanford University	None	None	None	None	None	None	None
Melissa Chan	BC Children's Hospital (Canada)	None	None	None	None	None	None	None
Sarah E. Haskell	University of Iowa	NIH (K08 Career Development in Zebrafish Cardiac Development)*	None	None	None	None	None	None
Mary Fran Hazinski	Vanderbilt University School of Nursing	None	None	None	None	None	American Heart Association Emergency Cardiovascular Care Programs†	None
Benny L. Joyner Jr	University of North Carolina	None	None	None	None	None	None	None
Javier J. Lasa	Texas Children's Hospital, Baylor College of Medicine	None	None	None	None	None	None	None
S. Jill Ley	American Association of Critical Care Nurses	None	None	None	None	None	None	None
Tia T. Raymond	Medical City Children's Hospital	NIH R01 (Optimized and Personalized Ventilation to Improve Pediatric Cardiac Arrest Outcomes [OPTI-VENT] [Studies in Neonatal and Pediatric Resuscitation])*; NIH R03 (The Impact on Outcomes of Emergency Medications at the Bedside in Pediatric Cardiac ICU Patients)*	None	None	None	None	None	None
Robert Michael Sutton	The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine	NHLBI (PI on CPR Quality Improvement trial)*	None	None	Roberts and Durkee†; Lowis and Gellen*; Donahue, Durham, and Noonan*	None	None	None
Alexis A. Topjian	The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine	NIH (subaward)*	None	None	Plaintiff*	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-mo period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Douglas Diekema	University of Washington	None	None	None	None	None	None	None
Elizabeth A. Greene	University of New Mexico	None	None	None	None	None	None	None
Justin M. Jeffers	Johns Hopkins University	None	None	None	None	None	None	None
Mary E. McBride	Lurie Children's Heart Center	None	None	None	None	None	None	None
Mark Meredith	University of Tennessee	None	None	None	None	None	None	None
Halden F. Scott	Children's Hospital Colorado	AHRQ (PI on a K08 from AHRQ studying prediction and diagnosis of pediatric septic shock. I do not directly receive personal funds from the grant.)*	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-mo period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.
* Significant.

analysis to examine the association of ECPR with favorable neurologic outcome in patients with IHCA of any origin.[38] During an 11-year period (January 2000–December 2011), 3756 patients were enrolled, with 591 receiving ECPR. Compared with conventional CPR, the use of ECPR was associated with higher favorable neurologic outcome at hospital discharge (odds ratio, 1.78 [95% CI, 1.31–2.41]).

A third study was a single-center retrospective review of patients with congenital heart disease who experienced cardiac arrest during cardiac catheterization.[39] During a total of 7289 cardiac catheterization procedures, 70 infants and children had cardiac arrest; of these, 18 (26%) received ECPR. The use of ECPR was associated with worse survival to hospital discharge compared with conventional CPR, although there was no adjustment for potential confounding variables.

The pediatric ILCOR systematic review and CoSTR[4,6] found no published studies reporting the outcomes after the application of ECPR for pediatric OHCA.

Recommendation—Updated 2019

1. **ECPR may be considered for pediatric patients with cardiac diagnoses who have IHCA in settings with existing ECMO protocols, expertise, and equipment (Class 2b; Level of Evidence C-LD).**

There is insufficient evidence to recommend for or against the use of ECPR for pediatric patients experiencing OHCA or for pediatric patients with noncardiac disease experiencing IHCA refractory to conventional CPR.

Discussion

The 2015 AHA PALS guidelines suggested that ECPR "be considered for pediatric patients with cardiac diagnoses who have IHCA in settings with existing ECMO protocols,

expertise, and equipment (Class IIb, LOE [Level of Evidence] C-LD)."[11] There were no prospective comparative analyses comparing survival and neurologic outcomes between conventional CPR and ECPR. This is not surprising given the potential ethical and logistical challenges in recruiting children for a prospective randomized trial during a cardiac arrest. However, data from large multicenter registry and retrospective propensity score analyses in child and adult populations suggest that ECPR may provide a significant survival benefit when used for refractory cardiac arrest.[38,40,41] Presumably, without ECPR, many of these patients would have died as a result of failed resuscitation attempts.

Current survival to hospital discharge rates for critically ill children experiencing IHCA resuscitated with conventional CPR range from 29% to 44%.[42,43] In contrast, recent ECPR studies of pediatric IHCA have reported survival to hospital discharge rates for mixed cardiac and noncardiac ICU populations as high as 48%.[32,44,45] Additional analyses reported that ECPR in the cardiac ICU was associated with higher survival to hospital discharge rates in patients with surgical cardiac disease compared with patients in the general ICU setting (73% versus 42%, respectively).[46–48] Our understanding of neurologic function after resuscitation with ECPR consists of single-center follow-up analyses[49,50] and the results of a randomized prospective trial of therapeutic hypothermia after IHCA.[51]

There is insufficient information about neurologic complications and outcomes (ie, hemorrhagic/ischemic stroke, seizure) associated with the use of ECPR in infants and children. In a multicenter randomized trial of therapeutic hypothermia after IHCA, only 30.5% of patients who received ECPR for IHCA had good neurobehavioral outcomes at 12 months of age.[51] In patients who received ECPR, therapeutic hypothermia, compared with normothermia, tended to be associated with lower survival with good neurobehavioral outcome at 1 year.[51]

Single-center analyses lack consistency in reported measures of neurologic function/status yet demonstrate favorable neurologic outcomes for the majority of survivors at follow-up (median range, 25–52 months).[49,50] Post–cardiac arrest care for patients undergoing ECPR should include ongoing surveillance for neurologic injury through the end of the ECMO course.

POST–CARDIAC ARREST TTM

TTM refers to continuous maintenance of patient temperature within a narrowly prescribed range. In initial studies of temperature management after cardiac arrest in adults[52] and after hypoxic-ischemic insult in neonates,[53] therapeutic hypothermia (32°C–34°C) was compared with standard (uncontrolled) temperature management that did not include fever prevention. In these early studies, fever in the control group may have contributed to worse outcomes and to the comparatively higher survival reported in the group treated with hypothermia. More recent studies compared what was described as therapeutic hypothermia (32°C–34°C) with controlled normothermia (36°C–37.5°C), with fever actively prevented.[16,54] These treatment modalities are now referred to as TTM 32°C to 34°C and TTM 36°C to 37.5°C, respectively.

Therapeutic hypothermia treats reperfusion syndrome after cardiac arrest by decreasing metabolic demand, reducing free radical production, and decreasing apoptosis.[55] It is not clear whether TTM to different temperature ranges has the same impact.

Evidence Summary—Updated 2019

The 2019 ILCOR pediatric CoSTR summarized the evidence supporting the use of TTM (32°C–34°C) after IHCA or OHCA in infants, children, and adolescents <18 years of age.[4,7] This pediatric review was triggered by the publication of the results of the THAPCA-IH trial (Therapeutic Hypothermia After Pediatric Cardiac Arrest In-Hospital), a randomized controlled trial of TTM 32°C to 34°C versus TTM 36°C to 37.5°C for IHCA.[54] Unlike previous ILCOR reviews and several earlier AHA PALS guidelines, the ILCOR pediatric CoSTR[4] and this 2019 PALS focused update are based only on evidence from pediatric studies; this update did not consider evidence extrapolated from adult studies. The writing group agreed that pediatric patients receiving TTM after cardiac arrest differ substantially from adult patients because infants and children have different causes of cardiac arrest, initial arrest rhythms, and techniques and equipment used for TTM, as well as differences in post–cardiac arrest care, compared with adults.

The THAPCA-IH trial was a large, multi-institutional, prospective, randomized controlled study of infants and children 2 days to 18 years of age. Methods and outcomes analyzed were identical to the 2015 THAPCA-OH trial (Therapeutic Hypothermia After Pediatric Cardiac Arrest Out-of-Hospital).[16] Both THAPCA studies evaluated the association between temperature targets and outcomes in children who received chest compressions for at least 2 minutes, were comatose (motor Glasgow Coma Scale score <5), and were dependent on mechanical ventilation after return of spontaneous circulation; both studies used the same protocol.[16,54] The only difference between the studies was the location of the arrest of the enrolled patients. The primary outcome evaluated for both trials was

favorable neurobehavioral outcome at 1 year, with secondary outcomes of survival at 1 year and change in neurobehavioral outcome. In both studies, temperature targets were actively maintained for 120 hours with the use of anteriorly and posteriorly placed automated cooling blankets. Temperature was continuously and centrally monitored. Patients in the TTM 32°C to 34°C group were cooled to a core temperature of 33°C (range, 32°C–34°C) with neuromuscular blockade and sedation for the first 48 hours. They were then rewarmed over a minimum of 16 hours and actively maintained at 36.8°C (range, 36°C–37.5°C) for the remainder of the study. Patients in the TTM 36°C to 37.5°C cohort received identical care except for a targeted temperature of 36.8°C (range, 36°C–37.5°C) for the entire 5-day intervention period.[16,54]

The THAPCA-IH trial was halted for futility after enrollment of 59% of targeted patients because the primary outcome (favorable neurobehavioral outcome at 1 year) did not differ significantly between the TTM 32°C to 34°C (36%, 48 of 133) and TTM 36°C to 37.5°C (39%, 48 of 124; relative risk, 0.92% [95% CI, 0.67–1.27]; P = .63) groups. Secondary outcomes, including a change in neurobehavioral outcome score by at least 1 SD from prearrest baseline at 1 year (30% versus 29%; P = .70), survival at 28 days (63% versus 59%; P = .40), and survival at 1 year (49% versus 46%; P = .56), did not differ between TTM groups. There were no significant differences between the temperature groups in the frequency of adverse events, including infection, need for transfusion, and serious arrhythmias within the first 7 days.[54]

The THAPCA-OH trial analyzed data from 260 patients. There was no significant difference in the primary outcome between patients treated with TTM 32°C to 34°C and those treated with TTM 36°C to 37.5°C (20% versus 12%; relative risk, 1.59 [95% CI, 0.89–2.85]). There were also no differences in secondary outcomes, including change in neurobehavioral scores from baseline, survival at 28 days, or survival at 1 year.[16]

Recommendations—Updated 2019

1. **Continuous measurement of core temperature during TTM is recommended (Class 1; Level of Evidence B-NR).**

2. **For infants and children between 24 hours and 18 years of age who remain comatose after OHCA or IHCA, it is reasonable to use either TTM 32°C to 34°C followed by TTM 36°C to 37.5°C or to use TTM 36°C to 37.5°C (Class 2a; Level of Evidence B-NR).**

There is insufficient evidence to support a recommendation about treatment duration. The THAPCA (Therapeutic Hypothermia After Pediatric Cardiac Arrest) trials used 2 days of TTM 32°C to 34°C followed by 3 days of TTM 36°C to 37.5°C or used 5 days of TTM 36°C to 37.5°C.

Discussion

Since publication of the 2015 PALS guidelines, an additional randomized controlled trial of TTM of comatose children after IHCA has been published.[54] This in-hospital study, from the same investigational team and with the same treatment protocol as the out-of-hospital study,[16] compared post–cardiac arrest TTM 32°C to 34°C with TTM 36°C to 37.5°C. Together, these trials form the basis of the current guidelines. Although several pediatric observational studies were also included in the ILCOR evidence review,[7] the observational studies had differing inclusion and exclusion criteria and varying protocols for temperature management, duration of TTM, and definitions of harm.[56–59] In addition, although there are several randomized controlled trials of TTM within the adult population, the ILCOR Pediatric Life Support Task Force and this writing group placed a higher value on pediatric data because the adult studies include patients with arrest causes, disease states, and outcomes that differ from those of children and thus would provide only indirect evidence.

Although there were no significant differences in outcomes between the 2 TTM groups in the THAPCA trials (ie, therapeutic hypothermia versus therapeutic normothermia), hypothermia has been shown to be advantageous in animal models and neonatal hypoxic injury and in mediating the adverse effects of the post–cardiac arrest syndrome. Given the severity of neurologic injury that many children demonstrate after resuscitation from cardiac arrest, cardiac arrest poses a substantial public health burden, representing large numbers of years lost, which makes potential interventions to improve neurologic injury and survival a critical priority.

Although interpretation of many studies of pediatric patients resuscitated from IHCA or OHCA is challenged by low-quality evidence in heterogeneous populations, most observational studies have yielded similar findings.[56–59] These studies used different control groups, arrest locations, age groups, causes of arrest, duration of TTM, and type of follow-up. Despite 1 small observational study of TTM in OHCA survivors demonstrating statistical improvement in neurologic recovery[59] and an observational study of IHCA demonstrating worse neurologic outcomes and survival after TTM,[56] the majority of studies have demonstrated no differences in ICU duration of stay, neurologic outcomes, and mortality with the use of therapeutic hypothermia versus controlled normothermia.

Both THAPCA trials[16,54] and 2 observational studies[60,61] used active

normothermia to maintain temperature below the febrile range. The other 7 observational studies[56–59,62–64] analyzed in the systematic review[3] did not control temperature in the control group; thus, there was a risk of fever that could have contributed to worse outcomes in the control group. This lack of temperature regulation in the control groups is a key limitation and a potential source of bias in these studies. Fever is common after a hypoxic-ischemic event such as cardiac arrest and has been shown from registry data to be associated with worse outcomes after cardiac arrest.[65] The negative results of recent TTM trials may be explained by the active maintenance of normothermia in control patients rather than a true noneffect of hypothermia. The early trials of hypothermia in both neonates and adults did not prevent fever, whereas later trials did.[53,66,67] A more recent TTM trial in neonates receiving ECMO used normothermic temperatures in the control group and did not demonstrate differences in outcomes or adverse effects.[68] Whether using TTM 32°C to 34°C followed by TTM 36°C to 37.5°C or using TTM 36°C to 37.5°C for infants and children who remain comatose after return of spontaneous circulation, the avoidance of fever is paramount.

Although these treatment recommendations apply to both OHCA and IHCA, it is important to recognize that outcomes of OHCA and IHCA differ in several key determinants. Response intervals are inherently longer for OHCA, as are the times to initiation of CPR, airway management, pharmacological therapies, and defibrillation. The presence of comorbidities, initial rhythms, and arrest causes all differ between children with OHCA and those with IHCA. However, because the conclusions of the 2 THAPCA trials[16,54] were the same, we have made a merged recommendation for both OHCA and IHCA.

The ILCOR pediatric ECPR systematic review included multiple subgroup analyses evaluating the critical outcomes of favorable neurobehavioral function and survival at multiple time points.[3] These subgroup analyses included location of arrest (OHCA versus IHCA), presumed cause of arrest (cardiac, asphyxial, drowning), and use of ECMO. Although no subgroup analysis was found to favor one treatment over another, the analyses were limited because only 1 randomized trial exists for each location, and the small sample sizes and lack of conformity within the observational trials prevented the pooling of data. Subgroup analyses of adverse events, including infection, serious bleeding, and recurrent cardiac arrest, were feasible from only the 2 randomized controlled trials. These studies found no statistical difference in positive outcomes or complications between TTM 32°C to 34°C and TTM 36°C to 37.5°C groups in either THAPCA trial.[16,54] Significant limitations persist even in the randomized trials, which affects the certainty of any recommendation about TTM during post–cardiac arrest care. Patient recruitment, especially in the randomized trials, occurred over many years, during which recommendations for CPR changed, including the recent changes to put greater emphasis on CPR quality. The exclusion criteria were extensive and may have excluded some patients who might have benefitted from TTM. Finally, and significantly, across the sites, there was no consistent use of a post–cardiac arrest care bundle such as identifying and supporting optimal blood pressure, metabolic or oxygen/ventilation targets, and methods of supportive care.

In the randomized trials,[16,54] the duration of TTM was 120 hours (5 days). In the observational trials, the duration of hypothermia varied from 24 to 72 hours.[56,58–64] Similarly, the duration of the rewarming period varied. Because no randomized trial tested the duration of TTM, the writing group felt that there was insufficient evidence to make a specific recommendation on this important aspect of the therapy.

Given the uncertainty of the effect of TTM, limitations of the data analysis, and lack of demonstrable harm, we agree that it is reasonable for clinicians to use TTM to 32°C to 34°C followed by TTM 36°C to 37.5°C or to use TTM 36°C to 37.5°C. Clinicians should consistently implement the strategy that can most safely be performed for a specific patient in a specific clinical environment. Regardless of strategy, providers should strive to prevent fever >37.5°C.

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